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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
09/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/814,749	CHARMOT ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,15,30,34,40,51-64,66-76 and 2129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,15,30,34,40,51-64,66-76 and 2129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 15, 21, 29, 30, 34, 51-59, 62-64, 66-73, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) in view of Cohen et al (USPN 6,558,665 hereafter '665). The claims are drawn to an oral formulation comprising core-shell particles wherein the core comprises a cation-exchange resin and the coating is hydrophobic.

The '494 patent discloses a particle formulation comprising a core and a coating where the core comprises a cation exchange resin and the coating does not disintegrate during passage through the intestinal tract of humans and where the membrane is more permeable to monovalent cations rather than bi-or higher cations (page 1, lin. 49-55). The particles can be mixed with sodium chloride as an excipient and administered orally as a foodstuff (page 2, lin. 54-60). The

particles are safe means of absorbing cations from the digestive tract, encapsulating the ions and removing them as waste from the body (page 2, lines 8-12). The cation exchange materials come from a wide range of sources and can include sulphonated crosslinked polystyrenes, polycarboxylates, polymaleinates, polyacrylates and polyphosphates (page 2, lin. 20-34). The cation exchange resin of the reference can be used to remove potassium ions from a variety of sources (page 3, lin. 10-12). The coatings include polyethyleneimine and known surfactants (page 2, lin. 42-45; example 2). The particles can be further coated with cellulose acetate a well known enteric polymer (example 1). The reference is silent to the specific monomers of the instant claims. The particles are microcapsules that range in size from 0.01-10 mm in size, with specific ranges of approximately 290 microns (page 2, lin. 41-42; Example 1). The particles can be formulated in various pharmaceutical forms including tablets, pills and capsules (page 3, lines 15-18). The thickness of the coating can be adjusted during the coating process, whether through fluidized bed coating or via interfacial polymerization. Coating thickness manipulation can be seen in the '665 patent.

The '665 patent discloses uniform coating surrounding particles (abstract). The coating is uniform from 10-20 microns thicken and can comprise a crosslinked polyethylene glycol (col. 7, lin. 15-20), along with other surfactants such as Poloxamer (col. 7, lin. 40-45). The coatings can be applied using interfacial polymerization (col. 7, lin. 58-60). Polystyrene particles measuring from 200-300 microns are coated with crosslinked polyethylene glycol at a thickness of 20 microns (example). That is a 0.1:1 ratio of components in order to achieve such as thickness and diameter. It would have been obvious to coat the particles of the '494 patent in a

similar fashion of the '665 patent since they both use the same method to apply uniform coatings. Also it would have been obvious since the '665 patent used surfactants as coating agents as well.

Regarding the percentages of retained potassium ions, it is the position of the Examiner that such percentages would be obvious in view of the prior art. It is the position of the Examiner that these retention percentages are merely functional limitations that are inherent to the components of the instant claims. The '494 and '665 patents discloses coated particles comprising polymeric cores comprising the same components as those recited in the claims, specifically crosslinked styrene or sulphonic polymers, coated by crosslinked synthetic polymers with polymerized ethylenic monomers. The coatings are applied in the same thickness and for the same purpose of removing cations from the digestive system. Specific cations include potassium. The combined disclosures meet the general conditions of the instant claims, and would inherently meet the functional limitations of the claims. Applicant is reminded that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

Regarding the condition the human patient is suffering for, it is the position of the Examiner that such limitations are merely a future intended use for the dosage form, and do not obviate over the prior art. As discussed above the prior art combination discloses the same oral pharmaceutical formulation comprising the same components. The prior art discloses a structurally identical pharmaceutical formulation comprising the same components, as such the condition suffered by the patient is irrelevant to the formulation itself. Inclusion of the condition adds an implicit method of administration step to the product claim, meaning the limitations are product-by-process claims.

The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. See *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. See *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983)

With these things in mind it would have obvious to coat the particles of the '494 patent in a uniform thickness as disclosed in the '665 patent. The patens disclose similar method of coating and comprise similar components, and as such it would have been obvious to coat the particles to a uniform thickness of 10-20 microns as disclosed in the '665 patent. One of ordinary skill in the art would have been motivated to combine the teachings disclosure and

suggestions of the prior art as such with an expected result of a stable coated cation exchange resin useful in removing cations from the intestinal tract of a human.

Claims 3, 34, 40 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) and Cohen et al (USPN 6,558,665 hereafter '665) in view of Chong et al (USPN 4,380,590 hereafter '590). The claims are drawn to a method of treating hyperkalemia in a human patient in need of treatment with a pharmaceutical formulation comprising core-shell particles with a specific configuration.

As disclosed as the '494/'665 patent combination discloses a pharmaceutical product useful in removing specific ions from the intestinal tract of humans. The ions removed depend on the cation exchange resin in the core. The ions removed can be sodium, potassium or ammonium. The reference is silent to specific disorders treated with this formulation; however it would be obvious to treat any conditions where ion reduction would be a treatment option.

The '590 patent discloses a cation exchange resin emulsion comprising a crosslinked copolymer component selected from the group consisting of styrene, vinyl, acrylic or methacrylic monomers (col. 5, lin. 15-52). Among the many uses for the cation exchange resin is a treatment for hyperkalemia (col. 9, lin. 35-55).

It would have been obvious to one of ordinary skill in the art to treat hyperkalemia with a cation exchange resin as disclosed in the prior art in order to sufficiently remove excess potassium ions from the body. Under the suggestion of the '590 patent to use acid cation ion exchange resins to treat hyperkalemia, the artisan of ordinary skill would have been motivated to

apply the composition of the '494/'665 patent combination in order to remove excess potassium ions from the body effectively treating hyperkalemia in a human patient in need of treatment.

Claims 3, 53, 60, 61, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) and Cohen et al (USPN 6,558,665 hereafter '665) in view of Shimzu et al (USPN 5,824,339 hereafter '339) and Macek et al (USPN 3,499,960 hereafter '960). The claims are drawn to a pharmaceutical formulation comprising core shell particles where the core is a cation exchange resin and the shell is a specific polymer.

As discussed above the combination of the '494/'665 patent discloses a pharmaceutical composition comprising core-shell particles with a desired shell and core. The combination is silent to the specific shell components of the instant claims. These shell components are well known in the art and would have been obvious additions. The combination discloses the use of crosslinked ethylic monomers in the shell, and suggests any useful polymer that can be made permeable to the desired valent cation is useful. These coating components can be found in the '339 and '960 patents.

The '339 patent discloses a core-shell particle formulation comprising a shell component comprising crosslinked polyvinylpyrrolidone, and a core comprising carboxyl functional groups (col. 8, lin. Lin. 14-25; col. 6, lin. 36-51). The core-shell particles further contain excipients and stabilizers to make them more palatable for oral administration (examples). The '960 patent discloses a palatable ion exchange formulation comprising a coating of crosslinked acrylic

polymers (abstract). The ion exchange resin includes crosslinked polystyrene resin and the coating is a crosslinked acrylic acid copolymer (col. 3, lin. 10-25).

It would have been obvious to include these shell components into the formulation of the '494/'665 combination in order to provide sufficient permeability of potassium ions into the cation exchange core. It would have been obvious to combine the teachings and suggestions in order to arrive at a palatable oral formulation useful in the treatment of a variety of ion related disorders.

Response to Arguments

Applicant's arguments filed 6/5/09 have been fully considered but they are not persuasive. Applicant argues that:

The combination of the '494 and '665 patents does not obviate the claims since they are nonanalogous art and do not solve the same problem.

Regarding this argument, it remains the position of the Examiner that the combination of the '494 and '665 patent continues to obviate the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the '665 patent is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977

F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the instant claims are drawn to a pharmaceutical composition comprising microparticles that are coated with a synthetic crosslinked polymer. The '665 patent explicitly discloses a microparticulate formulation comprising a core and coating where the coating is a crosslinked synthetic polymer. The coating is of the same thickness and composition of the instant claims. The coating is applied in order to provide s durable coating that does not disintegrate during use. This is the same utility as the instant claims and effectively solves the same problem. As such the '665 patent constitutes analogous art. Regarding the combination, the '494 patent discloses an oral pharmaceutical dosage form comprising a core and shell, where the core is a cation-exchange resin. The formulation is used to remove ions from a specific environment. The cores can be coated with any polymer. The microparticle is meant not to dissolve upon use. The '665 patent provides a stable and strong coating composition that prevents dissolution.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the increase selectivity of the coating to potassium over competing ions, or a coating that is designed to increase the amount of potassium) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant repeatedly argues that the '665 patent does not solve the problem of the instant claims namely applicant endeavor to develop an oral potassium binder with increased selectivity. However the claims do not recite this limitation and as previously argued the specification does not support such a limitation. The claims are drawn to a composition comprising coated microparticles

having a core and coating. The core is a cation exchange resin and the coating is a crosslinked polymer giving the coating a specific thickness. The '494 patent provides an oral composition comprising a coated ion exchange resin, where the coating is open to various well known polymers, and thickness of the coating can and should be controlled during processing. The patent discloses that the coating should not disintegrate and be more permeable to monovalent cations than to higher valances. The '665 patent provides a microparticle formulation comprising a crosslinked coating where the coating thickness is controlled through processing, and provides a stable protection for the core product. The '494 patent discloses that surfactants can be used as coating materials, and the '665 patent provides specific surfactants that are biocompatible polymers. These polymers are used to control entry of specific compounds into and out of the cell core (col. 8, lin. 20-58). The coatings of the '665 patent are used in a similar way to that of the '494 patent, namely permeability selection.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As can be seen the '494 patent provides a similar pharmaceutical composition as the instant claims where the core and coating is specifically designed to provide selective permeability. The '665 patent provides a specific coating material (suggested by the '494 patent)

that provides the same function as required by the '494 patent. The thickness can be controlled and is uniform despite the size do the core, meaning that permeability and transmission can remain constant and more controlled. For these reasons it would have been obvious to combine the prior art as described above. For these reasons the claims remain obviated.

The combination of the '494, '665 and '590 does not obviate the instant claims since the '590 patent does not address the problem of the instant invention.

Regarding this argument, it remains the position of the Examiner that the combination of the '494, 665 and 590 patents continue to obviate the instant claims. As discussed above the '494 and '665 combination discloses a pharmaceutical formulation comprising a core and coating where the coating is of a specific thickness in relation to the core and provides selective permeability to the core. Applicant argues that since the '590 patent does not address these issues, it does not obviate the instant claims. However the '590 patent is not applied to address these issues as they have been fully addressed and met by the combination of the '494 and '665 patents. The '590 patent is applied to show the level of skill in the art regarding the treatment of hyperkalemia. The '590 patent discloses a method of treating hyperkalemia using a liquid formulation comprising cation exchange resin emulsions. Addressing the limitations of claim 40, it would have been obvious to use the combination of the '494 and '665 patent to treat hyperkalemia since the combination would be a cation exchange rein and emulsions are suggested. For these reasons the claims remain obviated.

The combination of the '494, '665, '960 and '339 patents cannot obviate the instant claims since they do not address the same problem as the instant claims or invention.

Regarding this argument, it remains the position of the Examiner that the proposed combination would obviate the instant claims. As discussed above the '494/ '665 combination discloses a microparticulate formulation comprising coated ion exchange resin where the coatings regulate the permeability of ions to the core. This can be achieved by the material or the thickness. The thickness is controlled and manipulated to achieve optimum permeability via the thickness as disclosed in the '665 patent. The combination discloses a wide variety of polymers useful for coatings including polyethylene polymers and crosslinked block copolymers. The combination is silent to vinyl or acrylic polymers, however these polymers are common in the art as seen in the '960 and '339 patents. The '960 patent discloses coated ion exchange resin where the exchange resin comprises polystyrene copolymers and the coating is a crosslinked acrylic polymer. The coated resins are used to treat hypocholesteremia. The '339 patent discloses a core-shell polymer material that can comprise a variety of polymers that would coat the core including crosslinked polyvinylpyrrolidone. Applicant continue tot argue that these polymers would not address the inventions problem of allowing increased permeability of potassium to would. Again application is reminded that such a limitation is not present in the claims and is not supported by the specification. Assuming *en arguendo* that the claims required such a limitation, the '494 patent clearly discloses that the coating must allow for the permeability of lower valent ionic over higher valent ions.' The '665 patent further controls the permeability of the coating membrane by controlling the thickness of the coating and making it uniform for every particle. As such the problem of controlling the permeability of the outer

coating by controlling the thickness of the outer coating and by providing such a coating thickness and ratio to the core has been solved and addressed by the initial prior art combination of the '494 and '665 patents. The supporting patents merely show the level of skill in the art of microparticles, regarding the inclusion of acrylic and vinyl polymers. These polymers would be incorporated into the combination of '494 and '665 combination. Their thickness would be controlled through the process of the '665 patent and allow for a controlled permeability into the core as described in the '494 and '665 patents. This combination would have been obvious since each patent discloses similar coating materials such as polyethylene block copolymers and acrylic acid copolymers. For these reasons the claims remain obviated.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 8:00-5:30; every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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